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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/774,047	02/06/2004	Zhenwei Miao	4056.1066 US1	4991

38473 7590 07/24/2007

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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1624	

MAIL DATE	DELIVERY MODE
07/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/774,047	MIAO ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70 and 74-87* is/are pending in the application.

4a) Of the above claim(s) *4-14,17-20,23-26,33-64,74,76-77,80,83-84,86-87* is/are withdrawn from consideration.

5)☒ Claim(s) *27-31* is/are allowed.

6)☒ Claim(s) *1-3,15,16,21,65-70,75,78,81 and 82* is/are rejected.

7)☒ Claim(s) *22,32,79,and 81* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *November 28, 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of group I-1 in the reply filed on 6/14/2007 is acknowledged. The first traversal is on the ground(s) that unity of invention exists in the claims. This is not found persuasive because formula I, for example, does not have a definitive core. Variability in the core exists for variables j, m, s, and E. Variable j is any integer from 0-4, m is 0 to 2, s is 0 to 2, and E is either CH=CH or CH_2-CH_2. Based on the number of different combinations of these variables, there are 90 (5 x 3 x 3 x 2) possible core for formula I. The second traverse is in the ground that the restriction was based on what applicants prepared. This allegation is true because if applicants were given the choice of a catch-all group of compounds not covered by groups I-1 through XXXVIII—4 and chose that catch-all group, applicants would not be enabled for that group since applicants only prepared four different heterocycles for variable W, 2*H*-tetrazole, 1,2,3-triazole, bezotriazole, and pyridazin-2-one.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-3, 15-16, 21, 65-70, 75, 78, and 81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds where variable W is tetrazole, does not reasonably provide enablement for every single heterocycle encompassed by the provided definition in the specification, page 91, lines 23-26, as well as for prodrugs of compounds of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicants are enabled for compounds where variable W is defined as tetrazole, but are not enabled for compounds where variable W is every meaning encompassed by the definition of "heterocyclic"

which is defined as: "The terms "heterocyclo" and "heterocyclic" as used herein, refer to a monovalent substituent derived by removal of a hydrogen from a three to seven-membered saturated or unsaturated (including aromatic) cycle having 1 to 4 non-carbon ring atoms selected from the heteroatoms consisting of N, O, and S." Based on this definition, there are many possible heterocycles beside tetrazole. Prodrugs of the elected group and the species are not enabled because no prodrugs were actually prepared by applicants, only the exact compounds. In addition, a prodrug may be defined as "a precursor (forerunner) of a drug. A prodrug must undergo chemical conversion by metabolic processes before becoming an active pharmacological agent." ("Prodrug definition – Medical dictionary definitions of popular medical terms." https://www.medterms.com/script/art.asp?articlekey=23992, accessed July 11, 2007) Using this definition, a prodrug is *any* derivative of the claimed compounds that is produced in the process of the claimed compounds becoming pharmacologically active.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to macrocyclic peptidic compounds with a heterocyclic substituent attached to the proline portion of the macrocycle. Thus, the claims taken together with the specification imply the claimed compounds can treat hepatitis C virus (HCV).

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The elected group and species are considered novel.

(5) The relative skill of those in the art:

One of ordinary skill in the art is a chemist experienced in the synthesis of macrocyclic molecules through peptide couplings.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for claimed compounds where variable W is tetrazole.

However, the specification does not provide guidance for compounds with every possible example of heterocyclic ring encompassed by the definition of variable W. The specification also does not provide guidance for prodrugs of the claimed compounds.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the breadth of variable W and prodrugs of the claimed compounds, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

4. Claims 81-82 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In claim 81, formula VI is not the same formula as formula VI on page 41 of the specification. Similarly, formula VII in claim 82 is different from formula VII on page 42 of the specification.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 70 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply.

1. "Helicase" is vague: what kind of helicase is being referred to? Two examples of helicases are DNA helicases and RNA helicases.

2. "Polymerase" is vague: there is no mention in the specification to exactly what kind of polymerase is being referred to. Two examples of polymerases, among others are, DNA-directed DNA polymerase and DNA-directed RNA polymerases.

3. "Metalloproteases" is vague: Again, there is no definition of this term in the specification, and therefore it unclear what metalloprotease is being referred to. Is the metalloprotease a metalloendopeptidase or a metalloexopeptidase, for example?

4. "IRES" is not defined anywhere in the application, and its meaning cannot be determined as a result.

Claim Objections

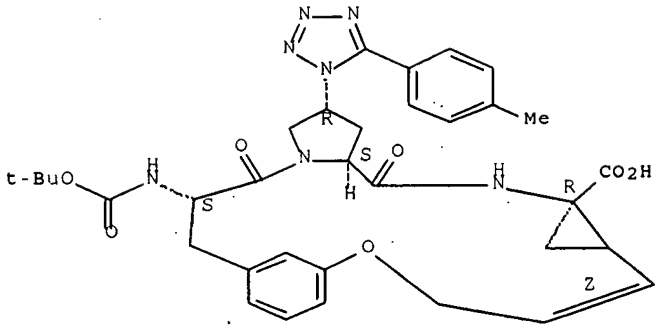
7. Claims 22, 32, 79, and 81 are objected to because they contain non-elected subject material.

8. Claim 32 is objected to because it has no period at the end of the claim. If this case becomes allowable, the examiner can correct this error.

Allowable Subject Matter

9. Claims 27-31 and 85 contain allowable subject matter.

10. The following is a statement of reasons for the indication of allowable subject matter: The closest art comes from Burger et al. (WO2007001406, published January 4, 2007), who report the structure below.



This structure does not read on the elected group because the phenoxy group cannot be part of the ring.

Conclusions

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on Monday-Friday from 7:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson, can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Noble Jarrell /NJ/

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